REMARKS

The Invention

The invention is generally directed to novel methods for identifying polypeptides that modulate gene expression from a promoter in a mammalian cell. These methods make use of the expression of anti-cell death proteins in a host mammalian cell to improve screening efficiency by reducing cellular toxicity resulting from the screening procedure.

The Office Action

Claims 1-44 are pending. Claims 5, 6, 17, 18, and 24-44 stand withdrawn as being directed to nonelected subject matter. The remaining claims stand rejected as being indefinite and as being obvious over Korsmeyer (U.S. Patent No. 5,834,209) in view of Kamb (WO98/36097). Each of these rejections is addressed in turn below.

Summary of the Amendments

Support for the amendments is found throughout the specification as filed. No new matter has been added.

New Claims 45-49

Applicants have added new claims 45-49. As is required by MPEP § 809.02(a), applicants point out that these new claims are readable upon the elected species.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 1-4, 7-16, and 19-23 are rejected as being indefinite. As discussed in detail below, applicants traverse this rejection as it applies to some of the rejections, and address the remaining rejections by amendment or cancellation of claims.

Claims 1 and 3

Claims 1 and 3 are rejected as being incomplete for omitting essential steps. According to the Office, the claims omit "the step by which increase or decrease in reporter gene is determined and the polypeptide identified." Applicants have amended claims 1 and 3 to remove the step of identifying a polypeptide that increases or decreases reporter gene expression, as previously recited in claims 1 and 3, respectively. As for the step by which reporter gene expression is determined, applicants submit that this is encompassed by step (b)—determining whether reporter gene expression is increased or decreased—and that no essential step is omitted. Determining whether reporter gene expression is altered requires the measurement of gene expression in the presence and absence of the library of polypeptides; this measurement can be performed using any appropriate method. As is taught at page 26, lines 10-13, reporter gene expression is measured "by assaying the RNA or protein levels." In sum, it is applicants' position that claims 1 and 3 recite all of the essential steps, and respectfully request that the rejection of these claims as being indefinite be withdrawn.

Claims 1 and 3 are further rejected under 35 U.S.C. § 112, second paragraph, for lacking antecedent basis for the term "promoter" and for reciting the conditional limitation "if" in the claims. Each of these rejections has been met by amendment.

Claims 2 and 4

Claims 2 and 4 are rejected as being indefinite for reciting the terms "more" and "less." Applicants respectfully traverse this rejection.

Applicants first note that the primary purpose of the § 112, second paragraph requirement is "to ensure that the scope of the claims is clear so the public is informed of the boundaries of what constitutes infringement of the patent." MPEP § 2173. "The essential inquiry pertaining to this requirement is whether the claims set out and circumscribe a particular subject matter with a reasonable degree of clarity and particularity." MPEP § 2173.02. As discussed below, the terms "more" and "less," when read in context of the claims, satisfy this test.

Claims 2 and 4 recite that the library of step (a) is divided into two or more libraries. One would readily recognize that the library may be divided to form two, three, four, or more libraries, after which time steps (a)-(c) are repeated until a polypeptide which increases (claim 2) or decreases (claim 4) reporter gene expression is identified.

The phrase "or more" is definite,[1] and withdrawal of this basis of the rejection is requested.

Claims 2 and 4 also recite that the two or more libraries have "less" complexity than that of the parent library. One or ordinary skill in the art of molecular biology would understand complexity to mean the number of different molecules in the library. This same person would also understand that a library having "less" complexity is one having fewer numbers of different molecules.

In sum, each of the terms "more" and "less" provides a reasonable degree of clarity and particularity to the claims and, thus, satisfies § 112, second paragraph.

Claim 2 is also rejected for recitation of the term "activates." Applicants have corrected this error by amendment.

Claim 7

Claim 7 is rejected for broadening the base claim (claim 1) with the recitation, in claim 7, of "expressing a library of DNA molecules in a cell." Applicants have amended this claim to recite that the library of DNA molecules is expressed in the cell which expresses the recombinant anti-cell death gene and that includes a reporter gene operably linked to the promoter. As amended, claim 7 is not broader than claim 1; rather it

[1] Applicants note that a search of the USPTO database identified more than 350,000 U.S. patents in which the phrase "or more" appeared in the claims. While recognizing that this observation is not dispositive, it nonetheless indicates that the phrase is generally recognized as having a definite meaning.

describes how, in claim 1, contacting step (a) is achieved. In view of this amendment, this rejection may now be withdrawn.

Claim 15

Claim 15 is rejected as being indefinite for reciting that the polypeptide is produced by a cell other than the cell that expresses the recombinant anti-cell death gene and that includes a reporter gene operably linked to the promoter. The Office appears to have two bases for rejecting this claim—the use of the term "other" and the alleged lack of clarity as to how the other cell produces the polypeptide. Applicants respectfully traverse this rejection.

Applicants first point out that a polypeptide that is employed in claims 45 or 46 (from which claim 15 now depends) can come from one of three sources—the cell that expresses the recombinant anti-cell death gene and that includes a reporter gene operably linked to the promoter; another cell (i.e., a cell other than the cell that expresses the recombinant anti-cell death gene and that includes a reporter gene operably linked to the promoter); or a source other than a cell. As is apparent from the foregoing, there can be no ambiguity as to the identity of the source of the polypeptide. How a cell produces a polypeptide would also be readily understood by one in the field of molecular biology. Endogenous or exogenous DNA is transcribed into mRNA, which is then translated into a polypeptide. The terms "other" and "produced by" provide a reasonable degree of clarity

and particularity to the claims, which is all that is required by MPEP § 2173.02, and thus satisfy § 112, second paragraph.

Claims 7-16 and 19-23

Claims 7-16 and 19-23 are rejected as being indefinite. These rejections are rendered moot by the cancellation of claims 13, 16, and 20, and the amendment of claims 7, 14, 15, 19, and 21-23 to remove reference to withdrawn claims.

Rejections under 35 U.S.C. § 103(a)

Claims 1-4, 7-16, and 19-23 are rejected as being obvious over Korsmeyer (U.S. Patent No. 5,834,209) in view of Kamb (WO98/36097). This rejection is respectfully traversed.

Korsmeyer describes a yeast two-hybrid screen in which a library of mammalian proteins fused to a transactivation domain are tested for their ability to bind to the anti-cell death protein Bcl-2 fused to a DNA binding domain. Intermolecular binding between the two fusion proteins leads to transcriptional activation of a reporter gene and identification of the protein capable of binding Bcl-2. The Kamb reference is directed to a method of identifying regulatory sequences that modulate gene expression; to that end, Kamb employs GFP as a reporter gene.

There would not have been a reasonable expectation that Korsmeyer's method, used solely in yeast cells, would work in mammalian cells. Thus, even if one would have

had a reasonable expectation that Kamb's reporter gene would function in Korsmeyer's yeast cell assay, as alleged by the Office, it would not follow that one would have a similar expectation that Korsmeyer's method would work in Kamb's mammalian cells, which is necessary to support a rejection of the claims as being obvious. As the presently amended claims now require the use of a mammalian cell, the rejection of these claims as being obvious over Korsmeyer in view of Kamb may be withdrawn.

Conclusion

Applicants submit that the claims are now in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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